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| **Identifying and differentiating lifelong FEV1/FVC and pre-COPD trajectories using biomarkers: a novel approach** |
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| **Background/aim**  Lifelong lung function trajectories may help identify a pre-clinical phase of COPD (Pre-COPD) and future COPD risk and prognosis. However, identifying lung function trajectories in clinical settings is not currently feasible, as repeated spirometry from childhood is rarely available. We aimed to investigate the ability of blood biomarkers, to differentiate lifetime obstructive lung function trajectories (i.e. detecting suboptimal trajectories and differentiating a relatively stable trajectory from progressive ones) in middle-aged Australians.  **Methods**  Lifetime FEV1/FVC trajectories were derived using Group-Based Trajectory Modelling (n=2442) using the Tasmanian Longitudinal Health Study (TAHS) lung function data from ages 7 to 53 years. Targeted biomarkers (CC16, sRAGE, CRP, ECP, SPD, Fibrinogen and cytokines from immunological pathways) were assessed at ages 45 and 53 years. Classification And Regression Tree (CART) analysis was used to investigate the ability of biomarkers to differentiate between FEV1/FVC trajectories, and a risk score chart was developed.  **Results**  From the six FEV1/FVC trajectories, all three obstructive trajectories (“Early low-rapid decline”, “Early normal-rapid decline” and “Early low-normal decline”) were at increased risk of COPD at 53 years. CC16, sRAGE, SPD and cytokine levels including IL-17a, IL-5 and IL-10 significantly differed between the three obstructive trajectories and the normal trajectory. Within the obstructive trajectories, these biomarkers also differentiated progressive (rapid decline) trajectories from relatively stable ones (normal decline). Different combinations of these biomarkers that predicted probabilities of different obstructive trajectories were identified and translated into a risk score chart that can be used to differentiate between rapid decline and normal decline obstructive trajectories.  **Conclusions**  Using a novel approach, this world-first study showed that common biomarkers, when assessed in middle age, were able to differentiate the lifetime rapidly progressive obstructive trajectories. Algorithms based on biomarkers and clinical information should now be developed for use in clinical practice to screen and optimise management of both Pre-COPD and COPD.  **Grant Support:** NHMRC; GSK; University of Melbourne |